

What is claimed is:

1. An inhibitor of histone deacetylase represented by formula (1):



wherein

- 5 Cy is cycloalkyl, aryl, or a radical of a heterocyclic moiety, any of which may be optionally substituted;

X is selected from the group consisting of C=O, C=CH₂, CH(OH), CH(OR¹), C=N(OH), and C=N(OR¹), where R¹ is alkyl, aryl, aralkyl, or acyl;

10 Y¹ is a C₃-C₇ alkylene, wherein said alkylene may be optionally substituted, and wherein one or two carbon atoms in the linear chain connecting X and W may be replaced with O, NR³, or S(O)_n, where R³ is hydrogen, alkyl, aryl, aralkyl, sulfonyl, acyl, alkoxy carbonyl, or carbamoyl, and n is 0, 1, or 2, provided that the atoms in Y¹ that are attached to X and to W are carbon atoms, and further provided that Y¹ does not comprise an ester or amide linkage in the linear chain connecting X and W; and

15 W is selected from the group consisting of -C(O)-CH₂-SR², -C(O)-NH-OM, -NH-C(O)-NH-Z, and -C(O)-NH-Z, where

R² is alkyl, aryl, aralkyl, or acyl, wherein the aryl portion of any such groups may be optionally substituted;

M is hydrogen or a pharmaceutically acceptable cation;

20 Z is selected from the group consisting of aniliny, pyridyl, thiazolyl, hydroxyphenyl, thiadiazolyl, anilinylmethyl, or pyridylmethyl, any of which groups optionally may be substituted with halo, hydroxy, amino, nitro, C₁-C₄ alkyl, or C₁-C₄ alkoxy;

provided that X is $C=CH_2$, $CH(OR^1)$, $C=N(OH)$, or $C=N(OR^1)$ when W is $-C(O)-NH-OM$ and Cy is unsubstituted phenyl, dimethylaminophenyl, or methoxyphenyl; and

further provided that when W is $-C(O)-CH_2-SR^2$, the carbon atom in Y^1 that is
5 attached to W is unsubstituted or is substituted with other than amino, acylamino, alkoxycarbonyl, or carbamoyl.

2. The inhibitor of claim 1, wherein Cy is C_6-C_{10} aryl or is a radical of a heterocyclic moiety selected from the group consisting of thiophene, benzothiophene, furan, benzofuran, pyridine, quinoline, indole, isoquinoline, thiazole, morpholine, piperidine, and piperazine, any of which groups may be
10 optionally substituted.

3. The inhibitor of claim 2, wherein the aryl or heterocyclic moiety is substituted by one or two substituents independently selected from the group consisting of C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_6-C_{10} aryl, heteroaryl, heterocyclyl, $(C_6-C_{10})ar(C_1-C_6)alkyl$, halo, nitro, hydroxy, C_1-C_6 alkoxy, C_6-C_{10} aryloxy, heteroaryloxy, C_1-C_6 alkoxycarbonyl, C_6-C_{10} aryloxycarbonyl, heteroaryloxycarbonyl, carboxy, and
15 amino.

4. The inhibitor of claim 1, wherein Cy has the formula $-Cy^1-Cy^2$ or $-Cy^1-G-Cy^2$, wherein Cy^1 and Cy^2 are independently C_3-C_6 cycloalkyl, C_6-C_{10} aryl, or a
20 radical of a heterocyclic moiety, which groups optionally may be substituted, and G is O, NR^3 , or $S(O)_n$, where R^3 is hydrogen, alkyl, aryl, aralkyl, sulfonyl, acyl, alkoxycarbonyl, or carbamoyl, and n is 0, 1, or 2.

5. The inhibitor of claim 4, wherein Cy^1 and Cy^2 are independently selected from the group consisting of phenyl, pyridinyl, morpholinyl, piperidinyl, piperazinyl, which groups optionally may be substituted.
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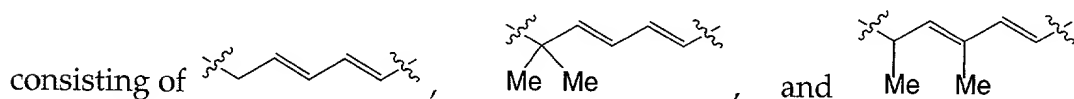
6. The inhibitor of claim 1, wherein X is selected from the group consisting of $\text{CH}(\text{OR}^1)$, $\text{C}=\text{N}(\text{OH})$, and $\text{C}=\text{N}(\text{OR}^1)$, where R^1 is $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_6\text{-C}_{10}$ aryl, or $(\text{C}_6\text{-C}_{10})\text{ar}(\text{C}_1\text{-C}_6)\text{alkyl}$.

7. The inhibitor of claim 1, wherein one to about three carbon atoms of the alkylene are independently substituted with halo, oxo, oximino, nitro, haloalkyl, alkyl, aralkyl, alkoxy, aryloxy, alkoxycarbonyl, carboxy, hydroxyalkyl, acyl, acyloxy, or cyano.

8. The inhibitor of claim 1, wherein Y^1 comprises an all-carbon linear chain connecting X and W.

9. The inhibitor of claim 8, wherein the linear chain connecting X and W comprises a dienyl moiety, wherein the dienyl moiety is attached to W.

10. The inhibitor of claim 9, wherein Y^1 is selected from the group



11. The inhibitor of claim 8, wherein Y^1 is $-(\text{CH}_2)_m$, where m is 5, 6, or 7.

12. The inhibitor of claim 1, wherein one carbon atom in the linear chain connecting X and W is replaced with O, NR^3 , or $\text{S}(\text{O})_n$.

13. The inhibitor of claim 12, wherein Y^1 is $-(\text{CH}_2)_n\text{-S}(\text{O})_n\text{-(CH}_2)_p$, where n is 0, 1, or 2, and p is 3, 4, or 5.

14. The inhibitor of claim 1, wherein W is $-\text{C}(\text{O})\text{-NH-OM}$, M being selected from the group consisting of hydrogen, sodium, potassium, magnesium, and calcium.

15. The inhibitor of claim 1, wherein W is -C(O)-NH-Z or -NH-C(O)-NH-Z, Z being unsubstituted 2-anilinyll or unsubstituted 2-pyridyl.

16. The inhibitor of claim 1, wherein W is -C(O)-CH₂-SR², R² being selected from the group consisting of C₁-C₆ alkyl, C₆-C₁₀ aryl, (C₆-C₁₀)ar(C₁-C₆)alkyl, (C₁-C₆ alkyl)carbonyl, (C₆-C₁₀ aryl)carbonyl, and ((C₆-C₁₀)ar(C₁-C₆)alkyl)carbonyl, wherein the aryl portion of any such groups may be optionally substituted.

17. The inhibitor of claim 16, wherein R² is selected from the group consisting of methyl, phenyl, benzyl, benzoyl, and acetyl.

18. An inhibitor of histone deacetylase represented by formula (2):



wherein

Cy is cycloalkyl, aryl, or a radical of a heterocyclic moiety, any of which may be optionally substituted;

Y² is C₅-C₇ alkylene, wherein said alkylene may be optionally substituted, and wherein one or two carbon atoms in the linear chain connecting Cy and W may be replaced with O, NR³, or S(O)_n, where R³ is hydrogen, alkyl, aryl, aralkyl, sulfonyl, acyl, alkoxycarbonyl, or carbamoyl, and n is 0, 1, or 2, provided that Y² does not comprise an ester or amide linkage in the linear chain connecting Cy and W; and

W is selected from the group consisting of -C(O)-CH₂-SR², -NH-C(O)-NH-Z, and -C(O)-NH-Z, where

R² is alkyl, aryl, aralkyl, or acyl, wherein the aryl portion of any such groups may be optionally substituted; and

Z is selected from the group consisting of anilinyll, pyridyl, thiazolyl, hydroxyphenyl, thiadiazolyl, anilinyllmethyl, or pyridylmethyl, any of which

groups optionally may be substituted with halo, hydroxy, amino, nitro, C₁-C₄ alkyl, or C₁-C₄ alkoxy;

provided that when W is -C(O)-CH₂-SR², the carbon atom in Y² that is attached to W is unsubstituted or is substituted with other than amino, acylamino, alkoxycarbonyl, or carbamoyl.

19. The inhibitor of claim 18, wherein Cy is C₆-C₁₀ aryl or is a radical of a heterocyclic moiety selected from the group consisting of thiophene, benzothiophene, furan, benzofuran, pyridine, quinoline, indole, isoquinoline, thiazole, morpholine, piperidine, piperazine, quinazolinone, benzotriazinone, phthalimide, and dioxobenzoisoquinoline, any of which groups may be optionally substituted.

20. The inhibitor of claim 18, wherein the aryl or heterocyclic moiety is substituted by one or two substituents independently selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₆-C₁₀ aryl, heteroaryl, heterocyclyl, (C₆-C₁₀)ar(C₁-C₆)alkyl, halo, nitro, hydroxy, C₁-C₆ alkoxy, C₆-C₁₀ aryloxy, heteroaryloxy, C₁-C₆ alkoxycarbonyl, C₆-C₁₀ aryloxycarbonyl, heteroaryloxycarbonyl, carboxy, and amino.

21. The inhibitor of claim 20, wherein Cy has the formula -Cy¹-Cy² or -Cy¹-G-Cy², wherein Cy¹ and Cy² are independently C₃-C₆ cycloalkyl, C₆-C₁₀ aryl, or a radical of a heterocyclic moiety, which groups optionally may be substituted, and G is O, NR³, or S(O)_n, where R³ is hydrogen, alkyl, aryl, aralkyl, sulfonyl, acyl, alkoxycarbonyl, or carbamoyl, and n is 0, 1, or 2.

22. The inhibitor of claim 21, wherein Cy¹ and Cy² are independently selected from the group consisting of phenyl, pyridinyl, morpholinyl, piperidinyl, piperazinyl, which groups optionally may be substituted.

23. The inhibitor of claim 18, wherein one to about four carbon atoms of the alkylene are independently substituted with halo, oxo, oximino, nitro, haloalkyl, alkyl, aralkyl, alkoxy, aryloxy, alkoxycarbonyl, carboxy, hydroxyalkyl, acyl, acyloxy, or cyano.

5 24. The inhibitor of claim 18, wherein one carbon atom in the linear chain connecting Cy and W is replaced with O, NR³, or S(O)_n.

10 25. The inhibitor of claim 19, wherein one carbon atom in the linear chain connecting Cy and W is replaced with NR³, where R³ is selected from the group consisting of C₁-C₆ alkyl, C₆-C₁₀ aryl, (C₆-C₁₀)ar(C₁-C₆)alkyl, (C₁-C₆ alkyl)oxycarbonyl, (C₆-C₁₀ aryl)oxycarbonyl, ((C₆-C₁₀)ar(C₁-C₆)alkyl)oxycarbonyl, (C₁-C₆ alkyl)carbonyl, (C₆-C₁₀ aryl)carbonyl, and ((C₆-C₁₀)ar(C₁-C₆)alkyl)carbonyl.

26. The inhibitor of claim 18, wherein one or two carbon atoms in the linear chain connecting Cy and W are replaced by O.

15 27. The inhibitor of claim 18, wherein W is -C(O)-NH-Z or -NH-C(O)-NH-Z, Z being unsubstituted 2-anilinyll or unsubstituted 2-pyridyl.

28. The inhibitor of claim 18, wherein W is -C(O)-CH₂-SR², R² being selected from the group consisting of C₁-C₆ alkyl, C₆-C₁₀ aryl, (C₆-C₁₀)ar(C₁-C₆)alkyl, (C₁-C₆ alkyl)carbonyl, (C₆-C₁₀ aryl)carbonyl, and ((C₆-C₁₀)ar(C₁-C₆)alkyl)carbonyl, wherein the aryl portion of any such groups may be optionally substituted.

20 29. The inhibitor of claim 28, wherein R² is selected from the group consisting of methyl, phenyl, benzyl, benzoyl, and acetyl.

30. An inhibitor of histone deacetylase represented by formula (3):



wherein

Cy is cycloalkyl, aryl, or a radical of a heterocyclic moiety, any of which may be optionally substituted, provided that Cy is other than dimethylaminonaphthyl when Y^3 is $-(CH_2)_3-$;

5 Y^3 is C_2-C_6 alkylene, wherein said alkylene may be optionally substituted with one or more substituents independently selected from the group consisting of halo, hydroxy, oxo, nitro, haloalkyl, alkyl, aralkyl, alkoxy, aryloxy, carboxy, hydroxyalkyl, acyl, acyloxy, and cyano; and

10 W is selected from the group consisting of $-C(O)-CH_2-SR^2$, $-C(O)-NH-OM$, $-NH-C(O)-NH-Z$, and $-C(O)-NH-Z$, where

R^2 is alkyl, aryl, aralkyl, or acyl, wherein the aryl portion of any such groups may be optionally substituted;

M is hydrogen or a pharmaceutically acceptable cation; and

15 Z is selected from the group consisting of aniliny, pyridyl, thiazolyl, hydroxyphenyl, thiadiazolyl, anilinylmethyl, or pyridylmethyl, any of which groups optionally may be substituted with halo, hydroxy, amino, nitro, C_1-C_4 alkyl, or C_1-C_4 alkoxy;

provided that Z does not have the formula $-(C_5H_3N)-NHC(O)-Y^3-NH-S(O)_2-Cy$.

20 31. The inhibitor of claim 30, wherein Cy is C_6-C_{10} aryl or is a radical of a heterocyclic moiety selected from the group consisting of thiophene, benzothiophene, furan, benzofuran, pyridine, quinoline, indole, isoquinoline, thiazole, morpholine, piperidine, and piperazine, any of which groups may be optionally substituted.

25 32. The inhibitor of claim 31, wherein the aryl or heterocyclic moiety is substituted by one or two substituents independently selected from the group

consisting of C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₆-C₁₀ aryl, heteroaryl, heterocyclyl, (C₆-C₁₀)ar(C₁-C₆)alkyl, halo, nitro, hydroxy, C₁-C₆ alkoxy, C₆-C₁₀ aryloxy, heteroaryloxy, C₁-C₆ alkoxycarbonyl, C₆-C₁₀ aryloxycarbonyl, heteroaryloxycarbonyl, carboxy, and amino.

5 33. The inhibitor of claim 30, wherein Cy has the formula -Cy¹-Cy² or -Cy¹-G-Cy², wherein Cy¹ and Cy² are independently C₃-C₆ cycloalkyl, C₆-C₁₀ aryl, or a radical of a heterocyclic moiety, which groups optionally may be substituted, and G is O, NR³, or S(O)_n, where R³ is hydrogen, alkyl, aryl, aralkyl, sulfonyl, acyl, alkoxycarbonyl, or carbamoyl, and n is 0, 1, or 2.

10 34. The inhibitor of claim 33, wherein Cy¹ and Cy² are independently selected from the group consisting of phenyl, pyridinyl, morpholinyl, piperidinyl, piperazinyl, which groups optionally may be substituted.

15 35. The inhibitor of claim 30, wherein Y³ is a C₂-C₆ alkylene optionally substituted with one or two non-hydrogen substituents independently selected from the group consisting of halo, hydroxy, oxo, nitro, (halo)₁₋₅(C₁-C₃)alkyl, C₁-C₆ alkyl, (C₆-C₁₀)ar(C₁-C₆)alkyl, C₁-C₆ alkoxy, C₆-C₁₀ aryloxy, carboxy, hydroxy(C₁-C₆)alkyl, C₁-C₆ alkylcarbonyl, C₆-C₁₀ arylcarbonyl, C₁-C₆ alkylcarbonyloxy, C₆-C₁₀ arylcarbonyloxy, and cyano.

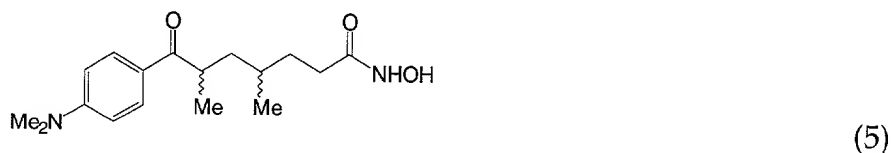
20 36. The inhibitor of claim 33, wherein Y³ is an optionally substituted saturated C₄-C₅ alkylene.

 37. The inhibitor of claim 30, wherein W is -C(O)-NH-OM, M being selected from the group consisting of hydrogen, sodium, potassium, magnesium, and calcium.

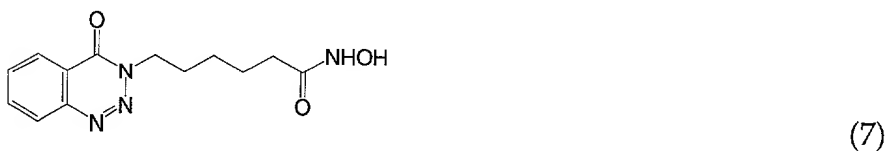
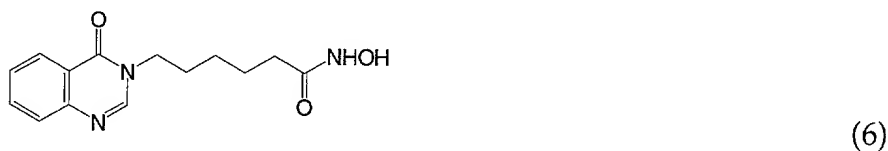
38. The inhibitor of claim 30, wherein W is -C(O)-NH-Z or -NH-C(O)-NH-Z, Z being unsubstituted 2-aniliny1 or unsubstituted 2-pyridyl.

39. The inhibitor of claim 30, wherein W is -C(O)-CH₂-SR², R² being selected from the group consisting of C₁-C₆ alkyl, C₆-C₁₀ aryl, (C₆-C₁₀)ar(C₁-C₆)alkyl, (C₁-C₆ alkyl)carbonyl, (C₆-C₁₀ aryl)carbonyl, and ((C₆-C₁₀)ar(C₁-C₆)alkyl)carbonyl, wherein the aryl portion of any such groups may be optionally substituted.

40. An inhibitor of histone deacetylase represented by one of formulae (4)-(5):



41. An inhibitor of histone deacetylase represented by one of formulae (6)-(7):



42. A pharmaceutical composition comprising an inhibitor of histone deacetylase represented by formula (1):



wherein

Cy is cycloalkyl, aryl, or a radical of a heterocyclic moiety, any of which may be optionally substituted;

5 X is selected from the group consisting of C=O, C=CH₂, CH(OH), CH(OR¹), C=N(OH), and C=N(OR¹), where R¹ is alkyl, aryl, aralkyl, or acyl;

10 Y¹ is a C₃-C₇ alkylene, wherein said alkylene may be optionally substituted, and wherein one or two carbon atoms in the linear chain connecting X and W may be replaced with O, NR³, or S(O)_n, where R³ is hydrogen, alkyl, aryl, aralkyl, sulfonyl, acyl, alkoxy carbonyl, or carbamoyl, and n is 0, 1, or 2, provided that the atoms in Y¹ that are attached to X and to W are carbon atoms, and further provided that Y¹ does not comprise an ester or amide linkage in the linear chain connecting X and W; and

W is selected from the group consisting of -C(O)-CH₂-SR², -C(O)-NH-OM, -NH-C(O)-NH-Z, and -C(O)-NH-Z, where

15 R² is alkyl, aryl, aralkyl, or acyl, wherein the aryl portion of any such groups may be optionally substituted;

M is hydrogen or a pharmaceutically acceptable cation;

20 Z is selected from the group consisting of aniliny, pyridyl, thiazolyl, hydroxyphenyl, thiadiazolyl, anilinylmethyl, or pyridylmethyl, any of which groups optionally may be substituted with halo, hydroxy, amino, nitro, C₁-C₄ alkyl, or C₁-C₄ alkoxy; and

a pharmaceutically acceptable carrier, excipient, or diluent;

provided that X is C=CH₂, CH(OR¹), C=N(OH), or C=N(OR¹) when W is -C(O)-NH-OM and Cy is unsubstituted phenyl, dimethylaminophenyl, or methoxyphenyl; and

further provided that when W is $-C(O)-CH_2-SR^2$, the carbon atom in Y^1 that is attached to W is unsubstituted or is substituted with other than amino, acylamino, alkoxycarbonyl, or carbamoyl.

43. A pharmaceutical composition comprising an inhibitor of histone
5 deacetylase represented by formula (2):



wherein

Cy is cycloalkyl, aryl, or a radical of a heterocyclic moiety, any of which may be optionally substituted;

10 Y^2 is C_5-C_7 alkylene, wherein said alkylene may be optionally substituted, and wherein one or two carbon atoms in the linear chain connecting Cy and W may be replaced with O, NR^3 , or $S(O)_n$, where R^3 is hydrogen, alkyl, aryl, aralkyl, sulfonyl, acyl, alkoxycarbonyl, or carbamoyl, and n is 0, 1, or 2, provided that Y^2 does not comprise an ester or amide linkage in the linear chain connecting Cy and W; and

15 W is selected from the group consisting of $-C(O)-CH_2-SR^2$, $-NH-C(O)-NH-Z$, and $-C(O)-NH-Z$, where

R^2 is alkyl, aryl, aralkyl, or acyl, wherein the aryl portion of any such groups may be optionally substituted; and

20 Z is selected from the group consisting of aniliny, pyridyl, thiazolyl, hydroxyphenyl, thiadiazolyl, anilinylmethyl, or pyridylmethyl, any of which groups optionally may be substituted with halo, hydroxy, amino, nitro, C_1-C_4 alkyl, or C_1-C_4 alkoxy; and

a pharmaceutically acceptable carrier, excipient, or diluent;

provided that when W is $-\text{C}(\text{O})-\text{CH}_2-\text{SR}^2$, the carbon atom in Y^2 that is attached to W is unsubstituted or is substituted with other than amino, acylamino, alkoxycarbonyl, or carbamoyl.

44. A pharmaceutical composition comprising an inhibitor of histone
5 deacetylase represented by formula (3):



wherein

Cy is cycloalkyl, aryl, or a radical of a heterocyclic moiety, any of which may be optionally substituted, provided that Cy is other than dimethylaminonaphthyl
10 when Y^3 is $-(\text{CH}_2)_3-$;

Y^3 is C_2-C_6 alkylene, wherein said alkylene may be optionally substituted with one or more substituents independently selected from the group consisting of halo, hydroxy, oxo, nitro, haloalkyl, alkyl, aralkyl, alkoxy, aryloxy, carboxy, hydroxyalkyl, acyl, acyloxy, and cyano; and

15 W is selected from the group consisting of $-\text{C}(\text{O})-\text{CH}_2-\text{SR}^2$, $-\text{C}(\text{O})-\text{NH}-\text{OM}$, $-\text{NH}-\text{C}(\text{O})-\text{NH}-\text{Z}$, and $-\text{C}(\text{O})-\text{NH}-\text{Z}$, where

R^2 is alkyl, aryl, aralkyl, or acyl, wherein the aryl portion of any such groups may be optionally substituted;

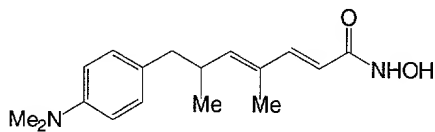
M is hydrogen or a pharmaceutically acceptable cation; and

20 Z is selected from the group consisting of anilinyll, pyridyl, thiazolyl, hydroxyphenyl, thiadiazolyl, anilinyllmethyl, or pyridylmethyl, any of which groups optionally may be substituted with halo, hydroxy, amino, nitro, C_1-C_4 alkyl, or C_1-C_4 alkoxy; and

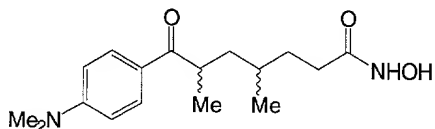
a pharmaceutically acceptable carrier, excipient, or diluent.

25 provided that Z does not have the formula $-(\text{C}_5\text{H}_5\text{N})-\text{NHC}(\text{O})-\text{Y}^3-\text{NH}-\text{S}(\text{O})_2-\text{Cy}$.

45. A pharmaceutical composition comprising an inhibitor of histone deacetylase represented by one of formulae (4)-(5):



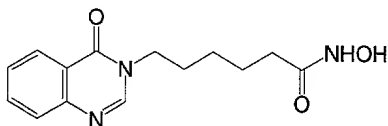
(4)



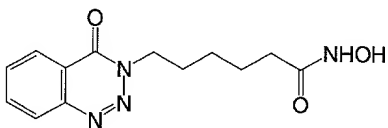
(5);

and a pharmaceutically acceptable carrier, excipient, or diluent.

46. A pharmaceutical composition comprising an inhibitor of histone deacetylase represented by one of formulae (6)-(7):



(6)



(7);

and a pharmaceutically acceptable carrier, excipient, or diluent.

47. A method of inhibiting histone deacetylase in a cell, comprising contacting a cell in which inhibition of histone deacetylase is desired with an inhibitor of histone deacetylase represented by formula (1):



wherein

Cy is cycloalkyl, aryl, or a radical of a heterocyclic moiety, any of which may be optionally substituted;

X is selected from the group consisting of C=O, C=CH₂, CH(OH), CH(OR¹), C=N(OH), and C=N(OR¹), where R¹ is alkyl, aryl, aralkyl, or acyl;

Y¹ is a C₃-C₇ alkylene, wherein said alkylene may be optionally substituted, and wherein one or two carbon atoms in the linear chain connecting X and W may be replaced with O, NR³, or S(O)_n, where R³ is hydrogen, alkyl, aryl, aralkyl, sulfonyl, acyl, alkoxycarbonyl, or carbamoyl, and n is 0, 1, or 2, provided that the atoms in Y¹ that are attached to X and to W are carbon atoms, and further provided that Y¹ does not comprise an ester or amide linkage in the linear chain connecting X and W; and

W is selected from the group consisting of -C(O)-CH₂-SR², -C(O)-NH-OM, -NH-C(O)-NH-Z, and -C(O)-NH-Z, where

R² is alkyl, aryl, aralkyl, or acyl, wherein the aryl portion of any such groups may be optionally substituted;

M is hydrogen or a pharmaceutically acceptable cation;

Z is selected from the group consisting of aniliny, pyridyl, thiazolyl, hydroxyphenyl, thiadiazolyl, anilinylmethyl, or pyridylmethyl, any of which groups optionally may be substituted with halo, hydroxy, amino, nitro, C₁-C₄ alkyl, or C₁-C₄ alkoxy;

provided that X is C=CH₂, CH(OR¹), C=N(OH), or C=N(OR¹) when W is -C(O)-NH-OM and Cy is unsubstituted phenyl, dimethylaminophenyl, or methoxyphenyl; and

further provided that when W is -C(O)-CH₂-SR², the carbon atom in Y¹ that is attached to W is unsubstituted or is substituted with other than amino, acylamino, alkoxycarbonyl, or carbamoyl.

48. A method of inhibiting histone deacetylase in a cell, comprising contacting a cell in which inhibition of histone deacetylase is desired with an inhibitor of histone deacetylase represented by formula (2):



wherein

Cy is cycloalkyl, aryl, or a radical of a heterocyclic moiety, any of which may be optionally substituted;

5 Y^2 is $\text{C}_5\text{-C}_7$ alkylene, wherein said alkylene may be optionally substituted, and wherein one or two carbon atoms in the linear chain connecting Cy and W may be replaced with O, NR^3 , or S(O)_n , where R^3 is hydrogen, alkyl, aryl, aralkyl, sulfonyl, acyl, alkoxycarbonyl, or carbamoyl, and n is 0, 1, or 2, provided that Y^2 does not comprise an ester or amide linkage in the linear chain connecting Cy and W; and

10 W is selected from the group consisting of $-\text{C(O)}-\text{CH}_2-\text{SR}^2$, $-\text{NH-C(O)}-\text{NH-Z}$, and $-\text{C(O)}-\text{NH-Z}$, where

R^2 is alkyl, aryl, aralkyl, or acyl, wherein the aryl portion of any such groups may be optionally substituted; and

15 Z is selected from the group consisting of anilinyll, pyridyl, thiazolyl, hydroxyphenyl, thiadiazolyl, anilinyllmethyl, or pyridylmethyl, any of which groups optionally may be substituted with halo, hydroxy, amino, nitro, $\text{C}_1\text{-C}_4$ alkyl, or $\text{C}_1\text{-C}_4$ alkoxy;

20 provided that when W is $-\text{C(O)}-\text{CH}_2-\text{SR}^2$, the carbon atom in Y^2 that is attached to W is unsubstituted or is substituted with other than amino, acylamino, alkoxycarbonyl, or carbamoyl.

49. A method of inhibiting histone deacetylase in a cell, comprising contacting a cell in which inhibition of histone deacetylase is desired with an inhibitor of histone deacetylase represented by formula (3):



25 wherein

Cy is cycloalkyl, aryl, or a radical of a heterocyclic moiety, any of which may be optionally substituted, provided that Cy is other than dimethylaminonaphthyl when Y³ is -(CH₂)₃-;

Y³ is C₂-C₆ alkylene, wherein said alkylene may be optionally substituted with one or more substituents independently selected from the group consisting of halo, hydroxy, oxo, nitro, haloalkyl, alkyl, aralkyl, alkoxy, aryloxy, carboxy, hydroxyalkyl, acyl, acyloxy, and cyano; and

W is selected from the group consisting of -C(O)-CH₂-SR², -C(O)-NH-OM, -NH-C(O)-NH-Z, and -C(O)-NH-Z, where

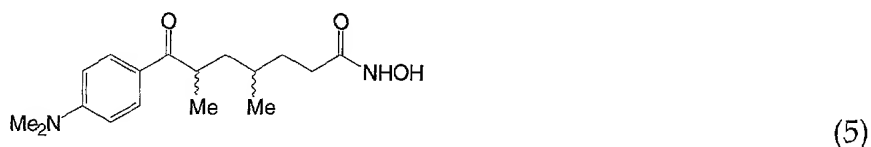
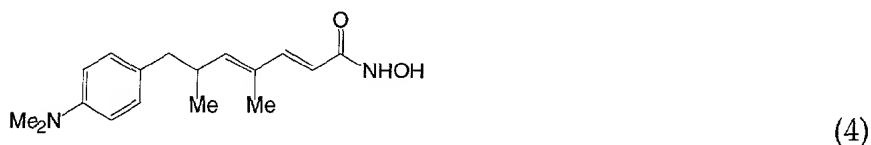
R² is alkyl, aryl, aralkyl, or acyl, wherein the aryl portion of any such groups may be optionally substituted;

M is hydrogen or a pharmaceutically acceptable cation; and

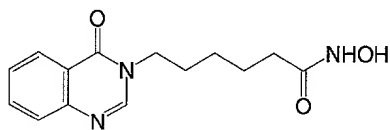
Z is selected from the group consisting of anilinyll, pyridyl, thiazolyl, hydroxyphenyl, thiadiazolyl, anilinyllmethyl, or pyridylmethyl, any of which groups optionally may be substituted with halo, hydroxy, amino, nitro, C₁-C₄ alkyl, or C₁-C₄ alkoxy;

provided that Z does not have the formula -(C₅H₃N)-NHC(O)-Y³-NH-S(O)₂-Cy.

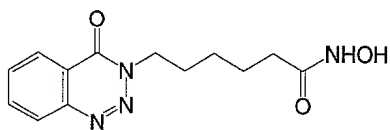
50. A method of inhibiting histone deacetylase in a cell, comprising contacting a cell in which inhibition of histone deacetylase is desired with an inhibitor of histone deacetylase represented by one of formulae (4)-(5):



51. A method of inhibiting histone deacetylase in a cell, comprising contacting a cell in which inhibition of histone deacetylase is desired with an inhibitor of histone deacetylase represented by one of formulae (6)-(7):



(6)



(7)

52. The method of any one of claims 47-51, wherein cell proliferation is inhibited in the contacted cell.

53. The method of any one of claims 47-51, wherein the cell is a neoplastic cell.

54. The method of claim 53, wherein the neoplastic cell is in an animal.

55. The method of claim 54, wherein the neoplastic cell is in a neoplastic growth.

56. The method of any one of claims 47-51, further comprising contacting the cell with an antisense oligonucleotide that inhibits the expression of a histone deacetylase.